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TITLE: Trials of Transcranial Stimulation for the Treatment of Parkinson's Disease

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14. ABSTRACT

During the first year of the study, we have been mainly working on the protocol "Transcranial Electrical Polarization for the Treatment of Bradykinesia and Rigidity in Patients with Parkinson's Disease". This is one of three protocols of the grant. This protocol was approved by the Office of Research Protections USAMRMC on 03/06/2007 Since then 3 patients were recruited in the protocol. The data was collected in 2 of them during the period of 8 TEP sessions. These patients are still in the protocol, and the data from them will be collected at 1 and 3 months follow up visits.

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Introduction

The treatment of Parkinson's disease (PD) needs further improvement, particularly in the areas of gait and freezing. Transcranial electrical polarization (TEP) which passes weak direct current (DC) current through the skull and across the cortex has been done for many years with numerous effects described in healthy subjects and patients with mental illness. Recent studies have demonstrated that anodal TEP (application of DC current) over the primary motor cortex (M1) produced sustained cortical excitability elevation measured by the amplitude of motor evoked potentiaks MEPs elicited by M1 TMS (Nitsche & Paulus 2000; 2001). Reversed polarity of the DC application resulted in opposite change of cortical excitability. fMRI demonstrated that cathodal polarization resulted in a global decrease of the mean number of activated pixels in M1 during sequential finger opposition test, while anodal polarization increased this number (Baudewig et al. 2001). The duration of the described effects is in the minutes range. Intriguingly, the behavioral effects reported in animals may persist for weeks (Hori & Yamaguchi 1975) and may occur with stimulation at microampere current intensity (Lu et al. 1994). The possibility of modulation of cortical excitability by TEP may be of some interest for the development of therapeutic interventions in patients with PD. This is of particular interest, taking into consideration hypoactivity of the supplementary motor area (SMA) in PD demonstrated in a variety of experimental approaches. fMRI (Tada 1998) and blood-flow PET studies (Playford et al. 1992; Jahanashahi et al. 1995) have revealed less SMA, putamen, anterior cingulate, and medial and dorsolateral prefrontal cortex activation in PD patients compared to matched controls. These hypoactive areas have been partially improved by apomorphine (Jenkins et al. 1992; Rascol et al. 1992). Therapeutic deep brain stimulation (DBS) of the STN enhanced movement-related activation in SMA, premotor cortex, and decreased M1 activation at rest (Limousin et al. 1997; Ceballos-Baumann et al. 1999) and influenced prefrontal BOLD activation (Sakatani et al. 1999).

TEP behavioral and electrophysiological effects in PD were studied in a pilot open research study in the Institute of the Human Brain of the Russian Academy of Sciences in St. Petersburg, Russia, resulting in the development of the method of treatment of PD by TEP (Lomarev et al. 1991). The study used the same TEP parameters as the current protocol in 42 patients with akinetic rigid form of PD, most of whom were also taking L-DOPA containing drugs (precursors of dopamine). In that pilot open design study, TEP improved bradykinesia and rigidity but not tremor in the majority of cases. This study used EEG and other electrophysiological methods to develop safe and effective TEP parameters and regimens (Lomarev 1989; 1996; Lomarev et al. 1991; 1993). Safe TEP parameters were found, which did not cause any significant side effects. They were characterized in terms of the most intense current, the longest session duration and the maximum number of sessions per week.

Body

During the first year of the study, we have been working mainly on the protocol "Transcranial Electrical Polarization for the Treatment of Bradykinesia and Rigidity in Patients with Parkinson's Disease". This is one of three protocols of the grant. This protocol was approved by the Office of Research Protections of the USAMRMC on 03/06/2007. Since then 3 patients were enrolled in the protocol. The data were collected in 2 of them during the period of 8 TEP sessions. The third patient was ineligible for this study due to arthritis and the associated pain. . This substantially influenced his gait, making the collected data unreliable. Participation in the protocol also caused undue risk and stress for this patient. Two patients remain in the protocol and the data from them will be collected at 1 and 3 months follow-up visits. One patient

experienced a headache 48 hours after the third placebo TEP session. No other adverse effects have been observed in these patients.

Before USAMRMC and Henry M. Jackson Foundation started financing the grant, 16 patients were enrolled in this protocol (NIH number 03-N-0116). Data have been collected (including 8 TEP sessions and 1 and 3 month follow-up visits) for 11 of them the.

Collected data were not analyzed since interim analysis is not stipulated for this protocol.

Key Research Accomplishments

Data have been collected for 13 patients under the protocol “Transcranial Electrical Polarization for the Treatment of Bradykinesia and Rigidity in Patients with Parkinson's Disease”.

Reportable Outcomes

At this point there is no reportable outcomes. Collection of the data is in progress.

Conclusion

The data have been collected under the first protocol of the grant.

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